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The molecular repertoire of macrophages in health and disease can provide novel biomarkers for diagnosis, prognosis, and treatment. Th2-IL-4-activated macrophages (M2) have been associated with important diseases in mice, yet no specific markers are available for their detection in human tissues. Although mouse models are widely used for macrophage research, translation to the human can be problematic and the human macrophage system remains poorly described. In the present study, we analyzed and compared the transcriptome and proteome of human and murine macrophages under resting conditions (M0) and after IL-4 activation (M2). We provide a resource for tools enabling macrophage detection in human tissues by identifying a set of 87 macrophage-related genes. Furthermore, we extend current understanding of M2 activation in different species and identify Transglutaminase 2 as a conserved M2 marker that is highly expressed by human macrophages and monocytes in the prototypic Th2 pathology asthma.